

**REMARKS**

Claims 1-16 are pending; claims 1-6 and 8-15 are rejected; claims 7 and 16 have been withdrawn from consideration.

Upon entry of this amendment claims 1-8, 10, 14 and 16 will be canceled, claim 17 will be added, and claims 9, 11-13, 15 and 17 will be pending.

Support for the amendment to claim 9 can be found in the specification at page 5, line 12, through page 7, line 2. Support for new claim 17 can be found at page 7, lines 10-21, and at page 52, lines 13-24

No new matter has been added. Entry of the Amendment is respectfully requested.

**I. Formal Matters**

Applicant notes that the Examiner has not yet acknowledged receipt of the certified copy of the priority document (filed in the international application), or Applicant's claim to priority in the instant application. Applicant respectfully requests that the Examiner acknowledge both receipt of the certified copy and Applicant's claim in the next paper issued by the Patent Office.

**II. Election/Restriction**

At page 2 of the Office Action, the Examiner indicates that Applicant elected the compound (I-1) without traverse, and that claims 7 and 16 are withdrawn as being drawn to a non-elected species.

While the Examiner states that compound (I-1) was elected without traverse, Applicant respectfully notes that the election without traverse was with respect to the restriction requirement as between the claims of Groups I and II. Indeed, as stated at pages 2-3 of the Office Action dated January 24, 2006, Applicant understands that the Examiner will expand the search to include all species encompassed by the generic formula recited in claim 9 upon finding that the method of treatment using compound (I-1) is novel.

Applicant thanks the Examiner for rejoinder of product claims of Group I (claims 1-8).

**III. Claim Rejection - 35 U.S.C. §101**

At page 3 of the Office Action, claim 10 has been rejected under 35 U.S.C. §101 as being drawn to non-statutory subject matter.

Included herewith is an amendment to the claims such that claim 10 has been canceled, thus making the rejection moot. In view of the cancellation of claim 10, reconsideration and withdrawal of this rejection is respectfully requested.

**IV. Claim Rejection - 35 U.S.C. §112**

A. At page 3 of the Office Action, claims 9-15 have been rejected under 35 U.S.C. §112, first paragraph, as being non-enabled.

The Examiner explains that while the specification is enabling for a method of treating a mouse asthma model with the elected compound to the extent that the number of eosinophils and neutrophils decreases, it does not reasonably provide enablement for the treatment and/or prevention of all allergic diseases, nor for the treatment without any specific endpoint with any EP3 receptor agonist for all mammals.

Included herewith is an amendment to the claims such that claims 10 and 14 have been canceled, thus making the rejection moot as to these claims. Also included herewith is an amendment to the claims such that claims 9, 11-13 and 15 now encompass a method for treating an allergic disease in a mammal using a small, well-defined genus of compounds.

In view of the amendment to the claims, the skilled artisan would be readily enabled to practice the full scope of the invention now recited in the claims. Accordingly, Applicant respectfully requests reconsideration and withdrawal of this rejection.

B. At page 7 of the Office Action, claims 1-6 and 8-15 have been rejected under 35 U.S.C. §112, first paragraph, as lacking adequate written description support in the specification.

The Examiner states that Applicant has not provided a description of the structure of a representative number of the compounds recited in the claims, nor a description of the chemical

and/or physical characteristics of a representative number of compounds, nor a description of how to obtain a representative number of specific compounds.

The Examiner also states with regard to claims 10-15 that there is insufficient evidence of a method for agonizing activity of an EP3 receptor in all situations comprising all possible compounds.

Included herewith is an amendment to the claims such that claims 1-6, 8, 10 and 14 have been canceled, thus making the rejection moot as to these claims. Also included herewith is an amendment to the claims such that claims 9, 11-13 and 15 now encompass a method for treating an allergic disease in a mammal using a small, well-defined genus of compounds.

The amended claims now recite a method of treating an allergic disease in a mammal that encompasses the use of a genus of compounds that are defined both functionally and structurally. The skilled artisan would readily understand that Applicant had possession of the complete scope of the method recited in the amended claims, and in particular, the entire genus of compounds encompassed by the claims.

In view of the amendment to the claims, and the comments above, the claims have adequate written description support in the specification as filed. Accordingly, Applicant respectfully requests reconsideration and withdrawal of this rejection.

C. At page 10 of the Office Action, claims 1-4 and 8-13 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner states that claims 1-4 and 8-13 are of indeterminate scope as the claims define the recited compounds by their function, and as the claims may encompass compounds not yet known or not yet understood.

Included herewith is an amendment to the claims such that claims 1-4, 8 and 10 have been canceled, thus making the rejection moot as to these claims. Also included herewith is an amendment to the claims such that claims 9 and 11-13 now encompass a method for treating an allergic disease in a mammal using a small, well-defined genus of compounds.

In view of the claim amendments, the claims are definite as written and Applicant respectfully requests reconsideration and withdrawal of this rejection.

**D.** At page 11 of the Office Action, claims 1-6 and 9-15 have been rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner states that the claim limitation “and/or” of claim 1 is indefinite. The Examiner also states that claim 10 is indefinite as it does not recite any active, positive steps delimiting how the recited use is practiced.

Included herewith is an amendment to the claims such that claims 1-6, 10 and 14 have been canceled, thus making the rejection moot as to these claims. Also included herewith is an amendment to claims 9, 11-13 and 15 to cancel recitation of “and/or” from the claims.

In view of the claim amendments, the claims are definite as written and Applicant respectfully requests reconsideration and withdrawal of this rejection.

**V. Claim Rejection - 35 U.S.C. §102**

At page 11 of the Office Action, claims 1-6 and 8 have been rejected under 35 U.S.C. §102(b) as being anticipated by EP 1 008 588, published June 14, 2000.

Included herewith is an amendment to the claims such that claims 1-6 and 8 have been canceled, thus making this rejection moot.

In view of the cancellation of claims 1-6 and 8, Applicant respectfully requests reconsideration and withdrawal of this rejection.

**VI. Claim Rejection - 35 U.S.C. §103**

At page 12 of the Office Action, claims 1-6 and 8-15 have been rejected under 35 U.S.C. §103(a) as being unpatentable over EP 1 008 588 in view of Sheller et al. (Sept. 2002).

The Examiner states that EP 1 008 588 teaches compound (I) and pharmaceutical compositions comprising compound (I). The Examiner notes that EP 1 008 588 does not teach that EP3 agonists are effective in treating allergies such as asthma.

The Examiner goes on to state that Sheller teaches that misoprostol is effective in treating atopic asthma, as recited in pending claims 8-15, via signaling through EP3 receptor.

The Examiner concludes that one of ordinary skill in the art would have been motivated to combine teachings of the cited publications because both are directed to agonizing EP3 and inhibition of prostaglandin E2. The Examiner further notes that Sheller teaches agonizing PGE2 receptors such as EP3 results in the reduction of IL-5 and, in turn, inflammatory cells, and that EP 1 008 588 teaches EP3 receptor is recognized as a receptor for PGE2.

Included herewith is an amendment to the claims such that claims 1-6, 8, 10 and 14 have been canceled, thus making the rejection moot as to these claims.

Applicant traverses the rejection of the remaining claims for the following reasons. Applicant first notes that while Sheller appears to teach that misoprostol is a PGE agonist that signals through EP3 receptor, and that misoprostol reduces airway IL-5 production (page 186, third paragraph), Sheller does not teach or suggest that an EP3 agonist can be used to treat an allergic disease, as recited in the pending method claims.

While eosinophils are inflammatory cells as noted by the Examiner, and IL-5 is a potent chemotactic and survival factor for eosinophils (page 190, last sentence), Sheller specifically states that misoprostol had no effect on the number of eosinophils, eosinophil cationic protein levels, or levels of cysteinyl leukotrienes (page 190, first paragraph).

Sheller also teaches that misoprostol is not an effective treatment of aspirin-sensitive asthma (page 191, lines 4-5), and that the effect of misoprostol on acute and late stage bronchoconstriction is unknown (page 191, lines 20-21).

Applicants further note that misoprostol is not specific for EP3 receptor, but also acts through EP2 and EP4 receptors (see Table 1 of enclosed paper by Kiriya et al., Br. J. Pharm. 122:217-224 (1997)).

No where is there a conclusion in Sheller that misoprostol was effective in treating an allergic disease. The authors do not extend their observations concerning the ability of misoprostol to reduce levels of IL-5 to the treatment of an allergic disease.

The Examiner has therefore not established a *prima facie* showing of obviousness. Neither EP 1 008 588 or Sheller teaches each and every limitation of claims 9, 11-13 and 15, namely, a method of treating an allergic disease using a compound of formula (I) of the pending application. While Sheller teaches that an EP3 receptor agonist can reduce IL-5 levels in a subject, there is no teaching that such reduction results in the treatment of an allergic disease as recited in claims 9, 11-13 and 15. While IL-5 is a selective eosinophil-activating growth hormone, and eosinophils are effectors of the immune system, eosinophils are also active in a variety of immune system functions, including host defense against parasitic infections. Therefore, the skilled artisan would understand that IL-5 inhibition would not inherently result in treatment of an allergic disease.

Furthermore, the skilled artisan would not have had a reasonable expectation of success in combining the teachings of EP 1 008 588 and Sheller. Again, as neither EP 1 008 588 nor Sheller teaches the treatment of an allergic disease, the skilled artisan would not have reasonably expected that the combined teachings could provide a method of treating an allergic disease. For the same reason the skilled artisan would not have been motivated to combine the teachings of the two publications to produce the claimed method.

As the Examiner has not established a *prima facie* showing of obviousness with respect to claims 9, 11-13 and 15, Applicant respectfully requests reconsideration and withdrawal of this rejection.

## **VII. Conclusion**

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

AMENDMENT UNDER 37 C.F.R. §1.111  
U.S. Appln. No. 10/530,752

Q87373

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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